REMARKS

Claims 1 and 18-21 are all the claims pending in the application.

Claim 20 has been amended to delete the recitation of "prevention" and to use the customary language for a method of treatment claim.

No new matter is added.

I. Formal Matters

Declaration of Translator

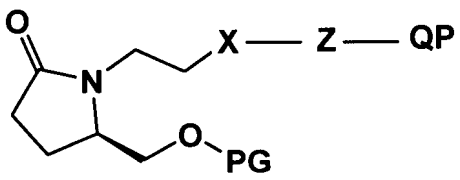
Submitted herewith is a Declaration of Translator to support the amendments of translation errors requested in the Response to Restriction Requirement and Preliminary Amendment filed November 6, 2006. See page 17, fifth full paragraph.

II. Detailed Action

A. Claim Rejections – 35 U.S.C. § 103

Claims 1, 18, 19, and 21 are rejected under 35 U.S.C.§103(a) as being unpatentable over Cameron et al., U.S. Patent No. 6,552,067.

The Examiner directs Applicant's attention to compound 2 at column 15:



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wherein PG is a protecting group, and the protecting group can be benzyl (Column 15, lines 25-26 and 37-39),

X is $-CH_2-$ or O (Column 4, lines 19-20),

Z is thienyl or thiazolyl (Column 4, lines 20-21), and

Q is carboxyl.

The Examiner further asserts that guided by the teachings of Cameron et al. one skilled in the art would be able to make similar prostaglandin antagonist [*sic.*, agonist] compounds by substituting sulfur for oxygen. The Examiner asserts that sulfur and oxygen are well known bioisosteres of one another. (the Examiner cites to Patani et al., Bioisosterism: A Rational Approach in Drug Design, Chem. Rev. 1996, 96, 3147-3176, especially page 3,156, which allegedly shows that sulfur and oxygen have similar bioactivity and, thus, are interchangable.) The Examiner states that the motivation would be to prepare similar compounds that are pharmacologically active as prostaglandin antagonists.

For the following reasons, this rejection is traversed, respectfully.

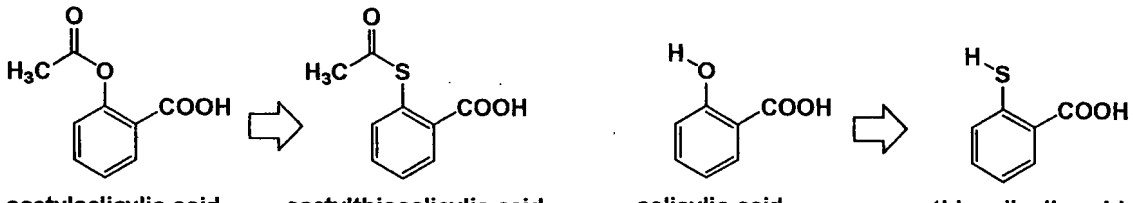
The compound that the Examiner relies upon is not disclosed as having any type of pharmaceutical activity. Rather, compound 2 of Cameron et al. is merely an intermediate for making the compound of formula (I), which is the compound that has pharmaceutical activity. Since there is no teaching in Cameron et al. that compound 2 has pharmaceutical activity, Applicant submits that there is no motivation to modify compound 2 to prepare similar compounds.

Furthermore, Patani et al. does not teach that S can be substituted for O and the same degree of activity will be retained.

More specifically, in Patani et al., the oral allergic activity of the compound having an "-O-" in its structure shows "+++ : activity grater than the positive control group" while that of the compound having a "-S-" in its structure shows only "+ : activity between positive and negative group". Namely, Patani et al., suggests that similar activity cannot be obtained by substitution of "-O-" with "-S-".

In this respect, the Examiner's attention is directed to Table 19 on page 3156 of Patani et al., submitted herewith.

As further evidence that "-S-" cannot similarly be substituted for "-O-", Applicant submits Journal of Pharmaceutical Science (1975), 64(5), 760-763 (Reference 1). As described in Tables 1 and 2 of this reference, acetylsalicyclic acid and salicylic acid have sedation activity for administration of Bradykinin. On the other hand, "isosteres" thereof, namely, acetylthiosalicylic acid and thiosalicylic acid which are compounds obtained by substituting "-O-" with "-S-" in acetylsalicylic acid and salicylic acid do not have the sedation activity and these compounds also exhibit toxicity.



acetylsalicylic acid acetylthiosalicylic acid salicylic acid thiosalicylic acid

Thus, the activity decreased or disappeared when the only difference was substitution of "-O-" with "-S-". Therefore, as a matter of course, "-O-" cannot be predictably substituted with "-S-".

Accordingly, claims 1, 18, 19 and 21 in the present application are not taught or suggested by Cameron since i) the compound represented by formula 2 is an "intermediate" without any disclosed activity, and ii) it is not predictable as to whether a compound in which "-O-" is substituted with "-S-" will have similar pharmacological activity tot eh parent compound. Therefore, there is no motivation to modify compound 2 of Cameron by substituting "-S-" for "-O-" in order to obtain a useful pharmaceutical.

B. Claim Rejections – 35 U.S.C. §112, 1st paragraph

Claim 20 is rejected under 35 U.S.C.§ 112, first paragraph, as failing to comply with the written description requirement because the specification allegedly does not enable one skilled in the art to treat dysmenorrheal and retinal neuropathy.

In analyzing the Wands factors, the Examiner in particular notes the lack of data demonstrating that the compounds are useful to treat the recited conditions.

As evidence that EP_2 agonists are considered useful to treat dysmenorrheal and retinal neuropathy, such as glaucoma, Applicant submits herewith four references.

An English translation of data in WO2004/0099117 (Reference 2) demonstrates activity of EP_2 agonists to suppress uterine contraction. See Example 1. Thus, the presently claimed compounds, which are EP_2 agonists, are useful to treat dysmenorrheal.

Nippon Ganka Gakki Zasshi. 1993 March; 97(3):289-96 (Reference 3), J. Ocul. Pharmacol. Ther. 1995 Fall; 11(3):447-54 (Reference 4), and US 5,877,211 (Reference 5), all demonstrate activity of EP_2 to depress intraocular pressure and protect the nerve. Thus, the presently claimed compounds, which are EP_2 agonists, are useful to treat retinal neuropathy.

Additionally, the fact that the compounds of the present application (for example, the compound described in Example 4(1)) have EP_2 binding activity is described in paragraph 0424 in US publication 2005/0124577. While the compound described in Example 4(1) is not included within the scope of the present claims, Applicant submits the following data on EP_2 binding activity of compounds within the present claims. The method for detection was the same as that described in paragraph 0416 to 0424 in US publication 2005/0124577A.

EP_2 binding activity

Example No.	Ki(nM)
	EP2
6(32)	0.5
6(48)	3.5
6(53)	1.0
6(60)	0.4
6(63)	0.4
6(74)	1.5
6(77)	0.4
6(89)	0.6

Accordingly, the compounds of the present application are effective for dysmenorrheal and retinal neuropathy since 1) EP_2 agonists are effective for dysmenorrheal and retinal neuropathy and ii) the compounds of the present application have EP_2 agonists activity.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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Date: April 20, 2007